UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/027,484	12/21/2001	Sebastian Bohm	TGZ-001B	9951

959 7590 04/19/2005

LAHIVE & COCKFIELD, LLP.
28 STATE STREET
BOSTON, MA 02109

EXAMINER	
BARTON, JEFFREY THOMAS	
ART UNIT	PAPER NUMBER
1753	

DATE MAILED: 04/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/027,484	Applicant(s) BOHM ET AL.	
	Examiner Jeffrey T. Barton	Art Unit 1753	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 January 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-69* is/are pending in the application.

4a) Of the above claim(s) *2-8,22-41,49-54,59,60 and 67-69* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,9-21,42-48,55-58 and 61-66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. The amendment filed on 27 January 2005 does not place the application in condition for allowance.

Status of Objections and Rejections Pending Since the Office Action of 27 October 2004

2. The objections to the drawings are withdrawn due to the submission of corrected drawing sheets and the amendment to the specification.

3. The objection to claim 56 is withdrawn due to Applicants' amendment.

4. The rejection of claim 65 under 35 U.S.C. §102(b) as anticipated by Howitz et al is maintained.

5. The rejection of claims 1, 42, 48, 56, 58, and 64 under 35 U.S.C. §102(b) as anticipated by Howitz et al is withdrawn due to Applicants' amendment.

6. The rejection of claims 9-12, 14, 15, 20, and 21 under 35 U.S.C. §102(b) as anticipated by Columbus (US 4,302,313) is withdrawn due to Applicants' amendment.

7. The rejection of claims 9, 10, 14, 15, 42, and 55 under 35 U.S.C. §102(b) as anticipated by Columbus (US 4,426,451) is withdrawn due to Applicants' amendment.

8. The rejection of claim 13 under 35 U.S.C. §103(a) as obvious over Columbus (US 4,302,313) in view of Columbus (US 4,426,451) is withdrawn due to Applicants' amendment.

9. The rejection of claims 16 and 17 under 35 U.S.C. §103(a) as obvious over Columbus (US 4,302,313) in view of Kopf-Sill is withdrawn due to Applicants' amendment.

10. The rejection of claims 16, 18, and 19 under 35 U.S.C. §103(a) as obvious over Columbus (US 4,302,313) in view of Swierkowski is withdrawn due to Applicants' amendment.

11. The rejection of claims 42, 43, 61, and 62 under 35 U.S.C. §103(a) as obvious over Sundberg et al in view of Howitz et al is withdrawn due to Applicants' amendment.

12. The rejection of claims 44 and 45 under 35 U.S.C. §103(a) as obvious over Sundberg et al in view of Howitz et al and Swedberg et al is withdrawn due to Applicants' amendment.

13. The rejection of claims 44 and 45 under 35 U.S.C. §103(a) as obvious over Howitz et al in view of Swedberg et al is maintained.

14. The rejection of claims 46, 47, 63, and 66 under 35 U.S.C. §103(a) as obvious over Howitz et al is maintained.

15. The rejection of claims 57, 61, and 62 under 35 U.S.C. §103(a) as obvious over Howitz et al in view of Sundberg et al is maintained.

Claim Objections

16. Claim 46 is objected to because it does not further limit the parent claim. A port with a dead volume of less than a picoliter, as recited in claim 42, will inherently have a dead volume less than a nanoliter. Appropriate correction is required.

Claim Rejections - 35 USC § 102

17. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

18. Claim 65 is rejected under 35 U.S.C. 102(b) as being anticipated by Howitz et al.

Regarding claim 65, Howitz et al disclose a method of injecting a second liquid into a microchannel filled with a first fluid, said method comprising: forming a droplet (5) from the second liquid, introducing said droplet through a virtual wall formed by the first fluid in a first fluid interface port (6) formed in a sidewall of the microchannel (9), wherein the microchannel is free of a second coaxially arranged fluid interface port formed in the sidewall at a location opposite to the first fluid interface port. (Column 2, line 65 - Column 3, line 34)

See arguments below for further discussion.

Claim Rejections - 35 USC § 103

19. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

20. Claims 1, 42, 46-48, 56, 58, 63, 64, and 66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Howitz et al.

Regarding claims 1 and 42, Howitz et al disclose a method of injecting a second liquid into a microchannel filled with a first liquid (Figure) comprising: forming a droplet

from the second liquid (Figure, droplet 5) and directing the droplet to, and introducing it through a virtual wall formed by the first fluid in a fluid interface port (6) formed in a sidewall of the microchannel (9). (Column 2, line 65 - Column 3, line 34)

Regarding claim 48, Howitz et al disclose the droplet traversing the virtual wall. (Column 3, lines 31-34) As such, its speed and direction must be appropriate.

Regarding claim 56, Howitz et al disclose fluid motion in the microchannel. (Column 2, lines 1-37)

Regarding claim 58, Howitz et al disclose a droplet having a diameter smaller than the fluid interface port. (Figure)

Relevant to claim 63, Howitz et al also suggest introduction of plural fluids through the interface ports of their device. (Column 1; repeated mention of a fluid microdiode permeable to *fluids* (italics added))

Regarding claim 64, Howitz et al disclose a method of injecting a second liquid into a microchannel filled with a first fluid, said method comprising: forming a droplet (5) from the second liquid, introducing said droplet through a virtual wall formed by the first fluid in a fluid interface port (6) formed in a sidewall of the microchannel (9), said fluid interface port having a diameter between about 25 μm and about 100 μm. (Column 2, line 65 - Column 3, line 34)

Howitz et al do not explicitly describe the dead volume within the interface ports or the introduction of a second droplet of a third fluid through a virtual wall in a second interface port.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method disclosed by Howitz by performing it in a device wherein the interface port has no dead volume (Claim 47) or dead volume of less than a picoliter (Other claims), because this dead volume is simply a function of the affinity of the fluid within the channel for the walls of the port, fluid surface tension, and the respective pressures of the liquid and gas at the interface. Howitz discusses such variability of meniscus formation (Column 3, lines 25-31), and choice of fluids, pressures, and materials would allow minimization or elimination of the dead volume.

Regarding claim 63, it would also have been obvious to one having ordinary skill in the art at the time the invention was made to use the invention of Howitz et al for the introduction of plural fluids to the fluid-filled channel, because it is suggested by Howitz et al and combination of multiple fluids is a common process requirement.

21. Claims 9-12, 14, 15, 20, and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Columbus (US 4,302,313) in view of Bjornson et al.

Relevant to claim 9, Columbus discloses a method of filling a microchannel, comprising directing fluid droplets through an interface port in the channel sidewall (Column 13, lines 30-34), such that the liquid traverses the port and enters the interior. (Column 13, line 42 - Column 14, line 16)

Relevant to claim 10, Columbus discloses the port being a filling aperture. (Column 13, lines 66-68)

Relevant to claims 11 and 12, Columbus discloses a pressure barrier formed in the microchannel to force the liquid in a first direction. (Figure 19, wider zones 220 force fluid to fill narrower portions of the channel) These widened portions can be called, "stopper holes."

Relevant to claim 14, Columbus discloses vent holes through the sidewall. (Column 14, lines 59-68)

Relevant to claim 15, Columbus discloses continued fluid introduction and transport until the channel is filled with liquid. (Figures 20a-c; Column 14, lines 22-40)

Relevant to claim 20, Columbus discloses filling the channel with two fluids introduced into separate filling apertures, each according to the method of claim 9. (Figures 20 a-c; Column 13, line 30 - Column 14, line 16) The sidewall of Columbus (e.g. Figure 2, plate 38) encompasses a hollow interior having a dimension (which reads on "diameter", since the channels are not limited to a circular shape) as low as 60 microns. (Column 7, lines 20-25)

Relevant to claim 21, Columbus discloses introduction of a gelatinous solution that would not be miscible with an introduced sample fluid. (Column 10, lines 4-41)

Columbus does not explicitly disclose a fluid interface port having a dead volume of less than a picoliter (Claims 9-12, 14, and 15), nor does he explicitly disclose the

filling apertures (e.g. 27) having diameters substantially equal to the "diameter" of the hollow interior.

Bjornson et al disclose a device with fluid transfer members (e.g. Figure 10) that comprise a plate (671) with thickness as low as 100 microns and an orifice (630) with diameter as low as 25 microns. (Column 11, lines 54-64; Column 22, lines 28-37) This would correspond to a port volume of about 50 picoliters. The range of orifice diameters preferred by Bjornson et al (Column 11, lines 54-64) includes the microscale dimensions the device of Columbus (Column 7, lines 20-25), and match typical channel dimensions within the system of Bjornson et al. (Column 8, line 64 - Column 9, line 4)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the device of Columbus et al by using thinner plate materials and smaller port diameters that substantially match channel dimensions, as taught by Bjornson et al, because miniaturization of these devices (Columbus is directed to electrochemical analysis of biological fluids) would allow the use of smaller sample volumes, the advantage of which would have been apparent to a skilled artisan at the time the invention was made, since miniaturization of sensors and fluid-handling devices has long been a goal within this art. A port dead volume of a picoliter or less would be present, dependent upon the affinities of the various surfaces for the fluid, surface tension, volume introduced, etc.

Specific to claims 20 and 21, selection of a suitable port size would have been a matter of choice to one having ordinary skill in the art.

Furthermore, Applicants' amendment introduces size limitations as bases for patentability. In *Gardner v. TEC Systems, Inc.*, 725 F.2d 1338, 220 USPQ 777 (Fed. Cir. 1984), *cert. denied*, 469 U.S. 830, 225 USPQ 232 (1984), the Federal Circuit held that, where the only difference between the prior art and the claims was a recitation of relative dimensions of the claimed device and a device having the claimed relative dimensions would not perform differently than the prior art device, the claimed device was not patentably distinct from the prior art device.

22. Claims 9, 10, 14, 15, 42, and 55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Columbus (US 4,426,451) in view of Bjornson.

Relevant to claim 9, Columbus discloses a method of filling a microchannel (Figures 1 and 2), comprising directing fluid droplets through an interface port in the channel sidewall (Column 5, lines 24-28), such that the liquid traverses the port and enters the interior. (Column 4, line 55 - Column 5, line 43)

Relevant to claim 10, Columbus discloses the port being a filling aperture. (Column 5, lines 24-28)

Relevant to claim 14, Columbus discloses vent holes through the sidewall. (Figure 2, hole 50)

Relevant to claim 15, Columbus discloses continued fluid introduction and transport until the channel is filled with liquid. (Figure 2, channel 22 is filled)

Relevant to claim 42, Columbus discloses introduction of a second fluid into a microchannel filled with a first fluid by directing a second liquid to a virtual wall formed in an interface port by the first fluid. (Figures 2-3; Column 7, lines 59-60)

Relevant to claim 55, Columbus discloses this second fluid being immiscible with the first. (Column 7, lines 59-60)

Columbus does not explicitly disclose a fluid interface port having a dead volume of less than a picoliter.

Bjornson et al disclose a device with fluid transfer members (e.g. Figure 10) that comprise a plate (671) with thickness as low as 100 microns and an orifice (630) with diameter as low as 25 microns. (Column 11, lines 54-64; Column 22, lines 28-37) This would correspond to a port volume of about 50 picoliters.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the device of Columbus et al by using thinner plate materials and smaller port diameters, as taught by Bjornson et al, because miniaturization of these devices (Columbus is directed to electrochemical analysis of biological fluids) would allow the use of smaller sample volumes, the advantage of which would have been apparent to a skilled artisan at the time the invention was made, since miniaturization of sensors and fluid-handling devices has long been a goal within

this art. A port dead volume of a picoliter or less would be present, dependent upon the affinities of the various surfaces for the fluid, surface tension, volume introduced, etc.

Furthermore, Applicants' amendment introduces a size limitation as a basis for patentability. In *Gardner v. TEC Systems, Inc.*, 725 F.2d 1338, 220 USPQ 777 (Fed. Cir. 1984), *cert. denied*, 469 U.S. 830, 225 USPQ 232 (1984), the Federal Circuit held that, where the only difference between the prior art and the claims was a recitation of relative dimensions of the claimed device and a device having the claimed relative dimensions would not perform differently than the prior art device, the claimed device was not patentably distinct from the prior art device.

23. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Columbus (US 4,302,313) and Bjornson et al as applied to claim 11 above, and further in view of Columbus. (US 4,426,451)

Columbus (US 4,302,313) and Bjornson et al disclose a combined method as described above in addressing claim 11.

Neither Columbus (US 4,302,313) nor Bjornson et al explicitly discloses disposition of a hydrophobic patch in the channel to form a pressure barrier (Claim 13).

Columbus (US 4,426,451) discloses using a hydrophobic surface to prevent fluid flow into a region of his device. (Column 8, line 54 - Column 9, line 22)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to further modify the method of Columbus (US 4,302,313) by performing it in a device that uses a hydrophobic surface to control fluid flow, as taught

by Columbus (US 4,426,451), because Columbus (US 4,426,451) teaches its effectiveness in preventing flow to undesired areas of the device, which is required in the method of Columbus. (US 4,302,313; Column 14, lines 29-40)

24. Claims 16 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Columbus (US 4,302,313) and Bjornson et al as applied to claim 9 above, and further in view of Kopf-Sill. (US 6,420,143)

Columbus and Bjornson et al disclose a combined method as described above in addressing claim 9.

Neither Columbus nor Bjornson et al explicitly disclose closing the fluid interface port after filling the channel (Claim 16) or closing the port with a fluid encapsulant. (Claim 17)

Kopf-Sill discloses sealing a fluid reservoir in a microfluidic device with mineral oil in order to reduce evaporative losses. (Column 8, lines 25-30)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to further modify the method of Columbus by adding a liquid encapsulant to the fluid inlet port to seal it after the fluid filling step, as taught by Kopf-Sill, because it would reduce evaporation losses and contamination in analyses run for a length of time or at a temperature where they would be a concern.

25. Claims 16, 18, and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Columbus (US 4,302,313) and Bjornson et al as applied to claim 9 above, and further in view of Swierkowski.

Columbus discloses a method as described above in addressing claim 9.

Columbus does not explicitly disclose closing the fluid interface port after filling the channel (Claim 16) or closing the port with a covering layer or adhered covering layer. (Claims 18 and 19)

Swierkowski discloses sealing fluid reservoirs in a microfluidic device with an adhesive film in order to reduce contamination and evaporative losses. (Column 2, line 67 - Column 3, line 9)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Columbus by covering the fluid inlet ports with an adhesive covering layer in order to seal them after the fluid filling step, as taught by Swierkowski, because it would reduce evaporation losses and contamination in analyses run for a length of time or at a temperature where they would be a concern.

26. Claims 42, 43, 61, and 62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sundberg in view of Bjornson et al and Howitz et al.

Relevant to claim 42, Sundberg et al disclose a method of introducing a fluid into a microchannel comprising forming a droplet of the fluid and introducing it to the channel via a fluid interface port. (e.g. Embodiment of Figures 2 and 3)

Relevant to claim 43, Sundberg et al disclose the fluid port comprising a second port arranged coaxially with the first, directly opposite. (Figures 2 and 3; Column 5, line 64 - Column 6, line 25)

Relevant to claim 61, Sundberg et al disclose forming the droplet on a droplet-carrying element. (Figure 2)

Relevant to claim 62, Sundberg et al disclose applying the droplet to the port with the droplet-carrying element.

Sundberg et al do not explicitly disclose the port having a dead volume of less than about one picoliter, the droplet being introduced through a virtual wall formed by a fluid already disposed within the channel, or the droplet being introduced to the virtual wall by the droplet-carrying element.

Bjornson et al disclose a device with fluid transfer members (e.g. Figure 10) that comprise a plate (671) with thickness as low as 100 microns and an orifice (630) with diameter as low as 25 microns. (Column 11, lines 54-64; Column 22, lines 28-37) This would correspond to a port volume of about 50 picoliters.

Howitz et al disclose addition of droplets of fluid through a virtual wall into a channel already filled with a fluid.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the device of Sundberg et al by using thinner plate

materials and smaller port diameters, as taught by Bjornson et al, because miniaturization of these devices would allow the use of smaller sample volumes, the advantage of which would have been apparent to a skilled artisan at the time the invention was made, since miniaturization of sensors and fluid-handling devices has long been a goal within this art. A port dead volume of a picoliter or less would be present, dependent upon the affinities of the various surfaces for the fluid, surface tension, volume introduced, etc.

etc.

It would also have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Sundberg et al by introducing the fluid via a virtual wall in the port into a channel already filled with fluid, as taught by Howitz et al, because it would allow facile dosing of additional liquids into the device.

Furthermore, Applicants' amendment introduces a size limitation as a basis for patentability. In *Gardner v. TEC Systems, Inc.*, 725 F.2d 1338, 220 USPQ 777 (Fed. Cir. 1984), *cert. denied*, 469 U.S. 830, 225 USPQ 232 (1984), the Federal Circuit held that, where the only difference between the prior art and the claims was a recitation of relative dimensions of the claimed device and a device having the claimed relative dimensions would not perform differently than the prior art device, the claimed device was not patentably distinct from the prior art device.

27. Claims 44 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sundberg et al, Bjornson et al, and Howitz et al as applied to claim 42 above, and further in view of Swedberg et al.

Sundberg et al, Bjornson et al, and Howitz et al disclose a combined method as described above in addressing claim 42.

None among Sundberg et al, Bjornson et al, or Howitz et al explicitly disclose any specific means of detection within their device.

Swedberg et al disclose a microfluidic device that includes apertures through the substrates that define the channels to enable optical detection. (Column 17, line 31 - Column 18, line 18)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the combined method of Sundberg et al, Bjornson et al, and Howitz et al by providing optical detection means with a beam directed at the aperture giving access to the channel interior, as taught by Swedberg et al, because such a beam path would minimize absorbance or distortion by the device material.

28. Claims 44 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Howitz et al in view of Swedberg et al.

Howitz et al disclose a method as described above in addressing claim 42.

Howitz et al do not explicitly disclose any specific means of detection within their device.

Swedberg et al disclose a microfluidic device that includes apertures through the substrates that define the channels to enable optical detection. (Column 17, line 31 - Column 18, line 18)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method disclosed by Howitz et al by providing optical detection means with a beam directed at the aperture giving access to the channel interior, as taught by Swedberg et al, because such a beam path would minimize absorbance or distortion by the device material.

29. Claims 57, 61, and 62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Howitz et al in view of Sundberg et al.

Howitz et al disclose methods as described above in addressing claim 42 and 56.

Howitz et al do not explicitly disclose causing fluid motion by electric fields (Claim 57), forming the droplet on a droplet-carrying element (Claim 61), or introducing the droplet to the virtual wall on a droplet-carrying element. (Claim 62)

Sundberg et al disclose fluid motion being caused by application of an electric field (Column 6, lines 26-33), formation of droplets on a carrying element prior to introduction to a channel (Figure 2), and introduction of the droplet to the port via the carrying element. (Column 5, lines 32-34)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method disclosed by Howitz et al by causing fluid

motion by application of an electric field, as taught by Sundberg et al, because it is a reliable means of causing fluid motion in a channel.

It would also have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method disclosed by Howitz et al by forming droplets on pins and introducing the droplets to the ports on these pins, as taught by Sundberg et al, because it is a controllable, reliable fluid transfer means.

Response to Arguments

30. Applicant's arguments, see the Amendment filed 27 January 2005, with respect to the rejections made in the previous office action have been fully considered and are partially persuasive. Most prior rejections have been withdrawn, as noted above. Some disagreement with respect to the claims and the prior art still exist, and Applicants' arguments, as they pertain to the currently applied rejections, are addressed below.

Regarding the teachings of Howitz et al, Applicant argues that the capillaries within the fluid microdiode they teach do not have a dead volume of less than one picoliter (Amendment, Page 15, 1st full paragraph) and that the menisci formed by the fluid at the ports of this device do not comprise "virtual walls" as defined in the specification. (Amendment, paragraph bridging Pages 15 and 16, Page 16, 1st full paragraph)

As was discussed in the prior office action (Page 13, 3rd paragraph), the Examiner considers the dead volume of this fluid microdiode to be variable, as is stated by Howitz et al. (Column 3, lines 25-31) The dead volume of the port will depend on the

affinity of the surface for the liquid in channel 9, pressure differences across the ports, etc. It is reasonable to expect that if the fluid within channel 9 does not wet the surfaces of the ports (i.e. is prevented from entering the port due to surface tension or energy considerations), the dead volume will be less than one picoliter or even approximately zero.

In the case that the liquid does not penetrate the capillaries, the Examiner further considers that the behavior of this meniscus as a "virtual wall" would naturally occur, as there would be no impediment to the liquid on the surface of the meniscus flowing with any net fluid flow in channels 7 and 9. In other words, there would be no apparent difference between the menisci of Howitz and the "virtual walls" of the instant application.

Although Howitz et al do not explicitly state that a dead volume less than one picoliter is attainable, one skilled in the art would certainly have realized that such a dead volume could be attained, depending upon selection of fluids, surface conditions, relative pressure within the capillary, etc., the variation of which would have been known and commonly performed by those having ordinary skill in the art.

Additionally, Applicants' amendment introduces size limitations as bases for patentability. As cited above, in *Gardner v. TEC Systems, Inc.*, 725 F.2d 1338, 220 USPQ 777 (Fed. Cir. 1984), *cert. denied*, 469 U.S. 830, 225 USPQ 232 (1984), the Federal Circuit held that changes in size alone do not provide patentability.

Applicants' arguments also include detailed descriptions, contrasting the methods of the instant application with those of Howitz et al, and enumerating the

advantages of the methods described in Applicants' specification. (Amendment, Page 15, 2nd full paragraph) While these may be correct, they do not correspond to limitations explicitly recited in the claims, and are therefore irrelevant.

Regarding the application of the Columbus '313 reference, Applicants argue that the reference does not teach the newly incorporated limitations regarding the dead volume (Claim 9) and the diameters of the ports (Claim 20). (Amendment, Page 16, 2nd and 3rd full paragraphs; Page 17, 1st paragraph) Examiner agrees that Columbus alone does not teach these limitations. However, the Examiner considers that the picoliter (or less) dead volume would result from the miniaturization of the dimensions of the device of Columbus et al, the feasibility of which is demonstrated by Bjornson et al, who demonstrated micron scale ports in thin plates as described above. As in the case of Howitz et al, the dead volume associated with these ports would vary depending on fluid and device properties, which would be a matter of selection to one having ordinary skill in the art.

Regarding the application of the Columbus '451 reference, Applicants argue that the reference does not teach the newly incorporated limitations regarding the dead volume (Claims 9 and 42). (Amendment, Page 17, 2nd and 3rd paragraphs) For the same reasons given above in discussing the Columbus '313 reference, the Examiner believes that this would result from the obvious miniaturization of the scale of the device components, as taught by Bjornson.

Regarding the prior rejections made under 35 U.S.C. §103(a), Applicant traverses on the same grounds discussed above, in that the references do not teach a

picoliter dead volume or virtual wall. (Note: Claim 20 had not been rejected under 103(a) previously) Applicant further asserts that Howitz requires a relatively large dead volume, which teaches away from the claimed invention. (Paragraph bridging Pages 17 and 18), and broadly asserts that no object reason for combination had been given in the prior action, and that a prima facie case of obviousness was therefore not made. (Page 18, 1st full paragraph) The Examiner does not consider Howitz et al to require a large dead volume. As discussed above, Howitz et al disclose variation in the position of the meniscus, which would allow a large, small, or even substantially nonexistent dead volume. Additionally, each previously made rejection under 35 U.S.C. §103(a) included corresponding reasoning, which is repeated in the new rejections, and such a broad assertion as that made by the Applicants is in no way persuasive.

Conclusion

31. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

32. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Jeffrey Barton, whose telephone number is (571) 272-1307. The examiner can normally be reached Monday-Friday from 8:30 am – 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nam Nguyen, can be reached at (571) 272-1342. The fax number for the organization where this application or proceeding is assigned is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free).

JTB
April 12, 2005

NAM NGUYEN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1700